Exhibit A

Abstracts from the American Society of Hematology
44th annual meeting December 2002

[609] Plant Derived Single-Chain Fv Idiotype Vaccines Are Safe and Immunogenic in Patients with Follicular Lymphoma: Results of a Phase I Study.

Sunil A. Reddy, Debbie Czerwinski, Ranjana Rajapaksa, Steve Reinl, Steve J. Garger, Terry Cameron, Julia Barrett, Jeanne Novak, R. Barry Holtz, Ronald Levy. Division of Oncology, Stanford Medical Center, Stanford, CA, USA; Large Scale Biology, Vacaville, CA, USA; Colorado Bioregistry; Evergreen, CO, USA

Idiotype vaccines for follicular B cell lymphoma are currently in phase III trials. However, the optimal vaccine formulation is still unknown. Novel strategies will continue to be explored in order to improve upon current protein vaccines. Areas in which improvements would be welcome include increasing the speed of vaccine production and maximizing immunogenicity. Towards this end, we have explored the use of idiotype vaccines produced in plants. This is the first report of the testing of a recombinant virus expressed, plant derived, autologous vaccine in humans. In this trial, single-chain Fv (scFv) idiotype protein vaccine was produced in the plant *Nicotiana benthamiana*, utilizing recombinant technology. The purpose of this phase I study was to explore the feasibility of scFv vaccine production, safety of vaccination, and measurement of immune responses in patients with follicular lymphoma who were in first chemotherapy induced remission. 16 patients were assigned to one of four treatment groups:

Table 1

	scFv Vaccine	scFv Vaccine + GM-CSF
Low Dose (0.2mg)	Group 1 (n=4)	Group 3 (n=4)
High Dose (2.0mg)	Group 2 (n=4)	Group 4 (n=4)

A total of six monthly treatments were planned for each patient. 15 of 16 planned patients have completed vaccination, with one patient showing progression of lymphoma before completion of the vaccine series. There were no significant toxicities or serious adverse events reported during the course of vaccine administration. 10 of 16 patients have developed immune responses to the vaccine. Both humoral and cellular responses were observed. Six patients developed specific cellular immune responses after vaccination: 4/8 in the GM-CSF arms (groups 3,4) versus 2/8 in the non GM-CSF arms (Groups 1,2). One group 4 patient received only 1 of 6 planned rounds of GM-CSF and did not make an immune response. There was no obvious advantage of the high dose (2.0 mg) as compared to the low dose (0.2mg) of vaccine. In conclusion, plant derived scFv idiotype vaccines are feasible to produce, safe to administer and can generate idiotype-specific immune responses. In contrast to previous vaccine formulations, no KLH conjugation was used in this study. A Phase II study utilizing an expanded cohort of patients with follicular lymphoma is planned.

Keywords: Follicular lymphoma\ Idiotype vaccines\ Single-chain Fv

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[2274] Enhanced In Vivo Response to an Idiotype Lymphoma Vaccine.
Alison McCormick, Terri Cameron, Fakhrieh Vojdani, Daniel Tuse. Large Scale Biology Corporation, Vacaville, CA, USA

B-cell lymphoma idiotype vaccines, where the tumor antigen is the surface Ig of the malignant B-cell clone, typically generate weak immune responses and often fail to induce protective immunity when administered singly as soluble proteins (Campbell et al., 1990, J. Immunol 145, 1029). Poor immunogenicity has been partially addressed by coupling the Ig to Keyhole Lympet Hemocyanin (KLH), a strongly immunogenic carrier. This technique has proven effective in both preclinical and human clinical trials (Hsu, et al., 1997, Blood 89, 3129; Bendandi et al., 1999, Nat Med 5, 171; Timmerman and Levy, 2000, J. Immunol 164, 4797). Another contributor to the poor immunogenicity of Ig idiotype vaccines may be related to the autologous constant region of the antibody, because immune tolerance can be partially overcome by grafting xenogeneic constant regions (Syrengelyas et al., 1996, Nature Med 9, 1038). We have studied a combination approach, removing the constant region completely and expressing only the tumor idiotype gene sequences as single-chain Fv (scFv) proteins using a plant virus-based transient expression vector in Nicotiana benthamiana host plants, and have evaluated the immunogenicity of these proteins with and without KLH conjugation. Previously we reported that strong protective immunity (80%) could be obtained when 15 mcg of 38C13 scFv protein was administered three times without adjuvant (McCormick et al, 1999, PNAS 96, 703). Here we report the results of a similar study using suboptimal doses of the vaccine, with or without KLH, using the 38C13 murine lymphoma model. Vaccinating twice with 1.5 mcg protein (1/10th the previously reported dosage used in multiple immunizations) coupled to KLH induced rapid and protective immune titers statistically similar to 38C13 Ig-KLH, with an overall survival rate of 70%. In a parallel experiment, a single dose of 15 mcg of the scFv-KLH conjugate gave significant survival (40%) compared to the Ig-KLH conjugate (50%), whereas at this dose the nonconjugated scFv protein failed to protect mice from lethal tumor challenge. In both experiments, high levels of IgG2 antibodies were measured in the sera of vaccinated mice. Our data suggest that Ig subunit vaccines can elicit superior immunogenicity and improved survival by removal of constant region and/or coupling to KLH for administration without adjuvant.
Keywords: Idiotype vaccine\ Plant scFv\ KLH conjugation

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[2994] Immune Cell Proteome: Proteomic Analysis towards the Identification of New Biomarkers for Hematopoietic Malignancies.

Thomas A. Davis, Sharon L. Wannberg, Anthony Makusky, Jeff Zhou, Tina Gatlin, Daniel Tuse. Immunology and Stem Cell Biology Program and Proteomics Department, Large Scale Biology Corporation, Germantown, MD, USA

Proteomics can be a valuable tool in the identification of proteins and biochemical pathways involved in hematopoietic malignancies. Protein-level profiling uniquely allows delineation of global changes in protein expression patterns resulting from transcriptional control, post-translational modifications, and redistribution of protein pools among cellular compartments. We developed and applied a variety of techniques, including cell type-specific immunoselection, rigorous sample processing, two-dimensional electrophoresis, mass spectrometry, and comprehensive data analysis, imaging and mining, with the goal of elucidating proteins and pathways deregulated in B-cell non-Hodgkin's lymphoma (NHL). Peripheral blood immune cells, platelets and malignant B-cells from lymph nodes of NHL patients were purified using positive immunomagnetic selection. Using 2-dimensional gel analysis, protein profile master patterns were generated for cytoplasmic and nuclear proteins. We successfully identified lineage-specific proteins and mapped differences in protein expression between peripheral blood WBC, mononuclear cells, neutrophils, monocytes, $CD19^+$ B cells, $CD4^+$ T cells, $CD8^+$ T cells, $CD83^+$ dendritic cells, platelets and lambda light chain-positive lymph node NHL B cells. Our techniques allowed the clear visualization of protein signals specific to malignant B cells (NHL tumor), manifested either as new, overexpressed or underexpressed relative to normal $CD19^+$ B-cell controls. Larger clinical sample sets, currently under quantitative analysis, may reveal whether these changes in protein profiles represent disease-specific markers. These findings from our large-scale protein discovery program may facilitate the development of novel classification schemes for staging of immune and hematopoietic cell disorders, the identification of novel markers for early diagnosis of malignant diseases, and the elucidation of prognostic indicators with clinical utility.
Keywords: Immune cell proteome\ Proteomics\ Non Hodgkins lymphoma